binding agent and said nucleic acid on said array surface;

whereby the presence of said analyte in said fluid sample is detected.

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 22-24 and 26-43 are pending after entry of the amendments set forth herein.

Claims 22-24 and 26-43 were examined. Claims 22-24 and 26-43 were rejected. No claims were allowed.

Please replace claims 22, 27, 31 and 34 with the clean version provided above.

Claims 22, 27, 31 and 34 have been amended to clarify that the claims are limited to methods of depositing a nucleic acid sample capable of hybridizing to a complement. Support for the amendments may be found on page 10 lines 20-27.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

No new matter has been added. As such, the Applicants respectfully request entry of the above amendments.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Rejection Under 35 U.S.C. § 102 (b)

Claims 22, 23, 26-31, 34, 37 and 38 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by U.S. Patent No. 5, 338,688 to Deeg *et al.* (hereinafter "Deeg").

As amended, Claims 22, 27, 31 and 34 are limited to methods of depositing nucleic acids in a manner such that the nucleic acids in the deposited fluid are capable of hybridizing to their complement.

It is well established that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art

reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987), *cert. denied*, 481 U.S. 1052 (1987).

Deeg describes the use of a thermal inkjet for the arrayed dispensing of biological molecules on a surface. The Examiner states on page 3 of the outstanding Office Action that Deeg teaches a method of depositing biochemical analytical chemical liquid, such as a protein, on a surface. Deeg, however, does not teach, or suggest, the use of the disclosed device in conjunction with nucleic acid molecules. Nowhere in Deeg is the term "nucleic acid" even employed. The illustrated examples in Deeg are limited to the arraying of dye reagents and small molecules such as enzymes, antibodies, and antigens. **As such, Deeg does not disclose the deposition of a nucleic acid onto a surface.**

The pending claims are all limited to deposition of nucleic acid containing fluids. Since Deeg does not even use the word "nucleic acid;" Deeg fails to teach this element of the claimed invention. As such, Deeg does not anticipate the claims of the present invention. Accordingly, Claims 22, 23, 26-31, 34, 37 and 38 are not anticipated by Deeg under 35 U.S.C. § 102 (b) and this rejection may be withdrawn.

Rejection Under 35 U.S.C. § 102 (e)

Claims 22, 23, 26-31, 34 and 37 have been rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent No. 5,958,342 to Gamble *et al.* (hereinafter "Gamble").

As noted above, Claims 22, 27, 31 and 34 have been amended to clarify that the claims are limited to methods of thermal ink jet depositing nucleic acid sample, where the deposited nucleic acids in the sample are capable of hybridizing to their complements. The cited reference, Gamble, fails to include this element of the present invention. Specifically, Gamble does not say anything regarding the successful use of thermal inkjet devices to deposit nucleic acid molecules. Therefore the reference cannot be found to anticipate these claims under 35 U.S.C. § 102 (e), and for this reason alone this rejection should be withdrawn.

Furthermore, in order for a disclosure to anticipate a claimed invention, the MPEP at § 2121 states that the cited disclosure must provide an enabling disclosure. Furthermore, the MPEP teaches that if a reference is relied upon as anticipating a claim, the Applicant may submit arguments establishing that the reference lacks an enabling disclosure and thereby rebut the presumption of operability of the cited reference and its anticipation of the claimed invention.

Under MPEP § 2121.01, the standard for determining whether a cited reference contains an enabling disclosure is if by way of the reference the public is in possession of the claimed invention. If one of ordinary skill in the art could have combined the reference's description with her own knowledge to produce the claimed invention, public possession of the invention has occurred. MPEP § 2121.01 (*citing In re* Donahue, 766 F.2d 531, 266 USPQ 619 (Fed. Cir. 1985)).

For the following reasons, the Applicants' submit the Gamble does not provided an enabling disclosure with respect to the use of a thermal inkjet to deposit nucleic acids onto a substrate surface.

Gamble describes the use of a jet droplet device to produce arrays of biological material. The disclosure provides that various transducers may be used for droplet formation, such as piezoelectric transducers and thermal transducers, such as a bubble-jet. Although the disclosure provides that both types of transducers may be used, **the illustrative examples are limited to piezoelectric transducers**. Gamble makes no showing of a successful application of thermal inkjet devices to deposit nucleic acids. As such, Gamble provides no working exemplification that thermal transducers can be employed to deposit nucleic acids.

Prior to the Applicants successful demonstration that the claimed methods actually work, the bare suggestion by Gamble to use a thermal jet device to deposit a nucleic acid did not provide an enabling disclosure because it did not place the claimed invention in the hands of the public. Gamble's bare suggestion failed to place the claimed invention in the hands of the public because of all of the different things that could have gone wrong with the claimed methods, such that one of skill in the art could not have had any reasonable expectation of success that the claimed invention would work prior to an actual working demonstration.

As evidence of this uncertainty with respect to the claimed methods, the Applicants cite U.S. Patent No. 5,658,802 to Hayes *et al.* (hereinafter "Hayes"). The Applicant, respectfully, disagrees with Examiner's comments on page 2 of the outstanding office action stating that Hayes provides one skilled in the art with guidance in reference to thermal inkjets and their application to the arraying of nucleic acid molecules. Hayes makes clear that thermal inkjets may be employed to deliver ink provided that the ink is controlled. As such, Hayes teaches one of skill in the art that thermal inkjets are very harsh on the deposited fluid, since concerns exists with regards to ink. Because ink is a much more stable substance than nucleic acids, it necessarily follows that one of skill in the art would have grave concerns as to the operability of such a system in depositing nucleic acids, since clearly all of the concerns about ink would be expected to be even greater with respect to a less robust fluid, such as a nucleic acid fluid. Specific problems that could have prevent the operability of the claimed methods include the extreme pressure, heat and force of ejection to which a nucleic acid fluid would be subjected. Such conditions could have been harmful and damaging to nucleic acid molecules, which could have resulted in breakage or sheering and therefore inoperability of the claimed methods.

Furthermore, the Hayes patent no. 5,658,802 in fact teaches away from the use of thermal inkjets for probe deposition:

> Although ejection devices based on any of the ink jet systems heretofore discussed might be used, continuous devices are typically more complex that drop-on-demand devices and **thermal devices are too harsh on the dispensed material**. Consequently, drop-on-demand devices are presently considered the most practical and have been found to accurately and repeatedly print drops of various fluids on solid substrates. Col. 3, lines 28-36.

Therefore, Hayes does in fact teach one of skill in the art that thermal devices are not appropriate for use with biopolymeric fluids, such as nucleic acid containing fluids.

As such, Gamble's disclosure does not place the claimed invention in the possession of the public because one of skill in the art would not have expected it to work, because of the

teaching of Hayes, prior to actual working exemplification, which was not provided by Gamble. As such, Gamble is non-enabling with respect to the disclosure of use of thermal inkjets for nucleic acid fluid deposition.

The Examiner attempts to rebut the evidence on non-enablement provided by the the Applicants by stating that a patent is presumed valid, and therefore this presumption overcomes the evidence of non-enablement provided by the Applicants. However, it is noted that only the claims in an issued patent are presumed valid. All of the claims in the Gamble patent are directed towards device claims. There are no method claims. As such, nothing in the claims indicates that a thermal inkjet is equal to a piezoelectric jet with respect to deposition of nucleic acids; therefore there is no reason to presume enablement for such a method exits in the Gamble patent. Furthermore, as indicated above, the Applicants have provided strong evidence to show that until one actually used a thermal inkjet to deposit nucleic acids, such an action would not be enabled because of all the existing uncertainty with respect to the success of the method. The Examiner's assertion of validity of a patent does not rebut this substantial evidence of non-enablement. In order to rebut the Applicants' provided evidence of non-enablement, the Examiner must provide evidence showing that, in fact, thermal inkjets have been used to successfully deposit nucleic acids and that the deposited nucleic acids are still capable of hybridizing to a complement. In the absence of such evidence, the Gamble reference is not enabling and therefore does not anticipate the claimed invention.

For the above provided reasons, Gamble fails to enable a method of using a thermal inkjet to deposit nucleic acids. Thus, the cited reference cannot anticipate the present invention. Since Gamble is non-enabling for a method in which a thermal inkjet device is suited to deposit nucleic acid molecules on a surface, Gamble fails to anticipate the claimed invention. Therefore, Claims 22, 23, 26-31, 34 and 37 are not anticipated under 35 U.S.C. § 102 (e) by Gamble and this rejection may be withdrawn.

Rejection Under 35 U.S.C. § 103 (a)

Claims 24, 32, 33, 35, 36 and 39-43 have been rejected under 35 U.S.C. § 103 (a) as being unpatentable over Gable or Deeg, either in view of U.S. Patent No. 6,132,030 to Cornell *et al.* (hereinafter "Cornell").

As discussed above, both Gamble and Deeg fail to anticipate the broadly claimed invention. Since Cornell has been cited solely for the μJ element, it fails to make up for this fundamental deficiency found in both Gamble and Deeg. Accordingly, applicant respectfully requests that the rejection of claims 24, 32, 33, 35, 36 and 39-43 as being obvious under 35 U.S.C. § 103(a) over Gamble or Deeg in view of Cornell be withdrawn.

Rejection Under 35 U.S.C. § 101

Claims 22, 23, 25, 26, 27-31, 34 and 37 have been provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 9, 10, 12-14, 16, 17, 20, 27 and 28 of copending Application No. 09/150,504.

The pending claims of 09/150,504 are directed to a method of depositing nucleic acid onto a substrate surface, i.e., to making an array. However, the claims of the present invention are directed to a method of depositing nucleic acid material, e.g., a sample, onto a surface, which already has a binding agent present, e.g. an array. For this reason, the Applicant respectfully requests that the present rejection towards the described invention be withdrawn.

Rejection Under Double Patenting

Claims 24, 33, 35, 36, 39 and 40 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9, 10, 12-14, 16, 17, 20, 27 and 28 of copending Application No. 09/150,504.

As stated above, the claims of the present invention are directed to a method of depositing nucleic acids onto a surface, which has a binding agent already present, e.g., an

array, as distinguished from the claims of the 09/150,504 application, which are directed to depositing nucleic acids on a ligand free substrate, e.g., methods of making an array. Therefore, the claims of the present invention and 09/150,504 are patentably distinguishable. For this reason, the Applicants respectfully request that the present rejection towards the described invention be withdrawn.

Conclusion

The applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Gordon Stewart at 650 485 2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: 6.10.02

By: _____
Bret E. Field for Gordon Stewart
Registration No. 37,620

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

22. (Amended) A method for depositing a quantity of fluid containing a nucleic acid, on a substrate surface having a plurality of binding agents stably associated therewith, said method comprising:

positioning a thermal inkjet head filled with said nucleic acid containing fluid in opposing relation to said substrate surface; and

actuating said thermal inkjet head in a manner sufficient to expel said quantity of fluid onto said substrate surface[; whereby] to deposit said quantity of fluid [is deposited] on said substrate surface, wherein nucleic acids present in said deposited fluid are capable of hybridizing to their complement.

27. (Amended) A method for depositing a quantity of fluid containing a nucleic acid or a polypeptide on an array surface, said method comprising:

loading said fluid into a thermal inkjet head comprising an orifice and a firing chamber by contacting said orifice with said fluid in a manner sufficient for said fluid composition to flow through said orifice into said firing chamber

positioning a thermal inkjet head filled with said fluid in opposing relation to said array surface; and

actuating said thermal inkjet head in a manner sufficient to expel said quantity of fluid onto said array surface[; whereby] to deposit said quantity of fluid [is deposited] on said substrate surface, wherein nucleic acids present in said deposited fluid are capable of hybridizing to their complement.

31. (Amended) A method for introducing a nucleic acid fluid sample to a binding agent, said method comprising:

positioning a thermal inkjet head filled with said nucleic acid fluid sample in opposing relation to a surface of an array, wherein said array comprises a plurality of binding agents stably associated with said surface;

actuating said thermal inkjet head in a manner sufficient to expel a quantity of

said fluid sample onto said array surface wherein nucleic acids present in said deposited fluid are capable of hybridizing to their complement; and

allowing interaction between said fluid sample and said binding agent.

34. (Amended) A method for detecting the presence of a nucleic acid in a fluid sample containing said nucleic acid, said method comprising:

positioning a thermal inkjet head filled with said fluid sample in opposing relation to a surface of an array, wherein said array comprises a plurality of binding agents stably associated with said surface and at least one of said binding agents specifically hybridizes to said nucleic acid;

actuating said thermal inkjet head in a manner sufficient to expel a quantity of said fluid sample onto said array surface wherein nucleic acids present in said deposited fluid are capable of hybridizing to their complement; and

detecting the presence of any binding complexes between said at least one binding agent and said nucleic acid on said array surface;

whereby the presence of said analyte in said fluid sample is detected.